Description

Microparticles produced from cycloolefin copolymers and their use for controlled active-substance release

The present invention relates to microparticles comprising cycloolefin copolymers, a process for their production, and their use for controlled release of active substances, preferably of agrochemicals, if desired using formulation auxiliaries or other auxiliaries, preferably diatomaceous earth.

In modern agrochemical technology more and more importance is placed on formulations and active-substance combinations used in forms which control their biodistribution and bioavailability.

Microparticles are used especially in the field of depot formulations, where the microparticle shell or matrix ensures that the release of the active substance present in the microparticles is delayed rather than immediate - known as controlled active-substance release or controlled release. Microparticles whose particle size is from 1 to 1000 μm are proving to be particularly promising formulations.

The controlled release, in particular of agrochemicals, over a prolonged period has a number of advantages. Firstly, repeated application of the agrochemicals can be reduced to one single application. Secondly, local over- and under-application can be avoided, as can rapid flushing out of the active substances or degradation of the same.

In the prior art, microsystems made from various materials and of various geometrical forms have been described. The production processes are similarly varied. Known systems include microcapsules made from polyethylene or from ethylene copolymers. Although ethylene-cycloolefin copolymers have been mentioned in connection

with microbeads these are for adhesives and powder paints (WO 97/48740) rather than for active-substance release. JP 05080232 describes the use of pure polynorbornenes for release of a perfume. A disadvantage is the high processing temperatures of homopolynorbornenes.

The prior art includes publications concerned with the release of active substances from ethylene (co)polymers. US 4,002,458 describes capsules with a core-shell geometrical form. Polyethylene shells are applied using a jet. This gives capsules of size up to 2 millimeters. Unlike with the core-shell geometric form, in the present invention the active substance has been embedded in a polymer matrix. Although ethylene-propylene copolymers are used in US 4,405,360, they are not used as particles but as flat-shaped dispensers. US 4,299,613 produces moldings from ethylene-vinyl acetate copolymers, but microparticles are not mentioned. EP 529975 describes the use of ethylene-vinyl acetate copolymers in the form of pellets. Polyethylene glycols are also mentioned relatively frequently (US 5,441,923), but these are water-soluble.

Microparticles for controlled active-substance release comprising cycloolefin copolymers have not been described in the prior art and in this connection represent a novel matrix material.

The advantages are seen as:

- Excellent biocompatibility and high purity of the polymers as matrix material, so that these materials can be used as basis materials for microparticles without endangering flora or fauna.
- The low content of double bonds susceptible to weathering gives the novel microparticles high storage stability.
- The high flowability of the basis material ensures that processing is relatively easy.

- The dimensional stability, mechanical strength, stiffness and hardness of the matrix materials gives improved handling of the novel microparticles.
- The microparticles are highly resistant to acids, alkalis and polar or moderately polar media, giving advantages in storage and handling
- The low density of the matrix material gives advantages in transport, storage and application.
- Since cycloolefin polymers have a variety of levels of heat resistance and their molar mass can be varied over a wide range, and their degree of crystallinity can be modified, the property profile of the matrix material can be matched to any particular application.

Surprisingly, experiments show that the desired controlled release of active substances from the advantageous matrix materials described is preferably brought about by formulation auxiliaries or other auxiliaries.

This is particularly surprising since the matrix materials of the novel microparticles are used as engineering plastics (e.g. Topas®).

The object of the present invention is therefore to provide microparticles comprising cycloolefin copolymers, preferably from ethylene-norbornene copolymers, as active-substance carriers for the controlled release of active substances, if desired using suitable formulation auxiliaries or other auxiliaries.

The object is achieved by means of microparticles which comprise cycloolefin copolymers, preferably ethylene-norbornene copolymers, and which, if desired using formulation auxiliaries or other auxiliaries, preferably diatomaceous earth, allow controlled release of the active substances.

The invention therefore provides microparticles obtainable from cycloolefin copolymers (termed "COC" below). The active substances have been embedded in a polymer matrix comprising at least one cycloolefin copolymer, preferably ethylene-norbornene-copolymers, and form a conglomerate (Figure 4). The invention therefore also provides a matrix of this type obtainable from at least one cycloolefin copolymer.

For the purposes of this invention, microparticle therefore means a product comprising matrix materials of the above polymers with an average diameter of from 1 to 1000 µm, preferably from 10 to 900 µm, particularly preferably from 50 to 800 µm and very particularly preferably from 100 to 600 µm. These are referred to above and below as novel microparticles.

The invention also provides the use of the novel microparticles as an active-substance carrier for the controlled release of active substances. For this, besides the active substances, formulation auxiliaries or other auxiliaries which permit controlled active-substance release may be introduced into the novel microparticles. Particular preference is given to diatomaceous earth or diatoms. Silica gel or any appropriate material known to the skilled worker may also be used in the same way. It is also possible to use inorganic substances of appropriate polarity and/or amorphicity, and substances of this type are expressly included. The formulation auxiliaries or other auxiliaries mentioned may also be used in combination with known formulation auxiliaries or other auxiliaries, such as cellulose, salts, etc.

In principle controlled active-substance release may also be obtained without any formulation auxiliary or other auxiliary, as can be seen from Fig. 1. This is particularly to be expected when the active substances inserted into the novel microparticles are hydrophobic.

By selecting and combining the matrix materials comprising

cycloolefin copolymers and in addition using formulation auxiliaries or other auxiliaries a wide range of possibilities can be opened up for controlled release of hydrophilic active substances.

For the purposes of the present invention, active substances are any biologically active substance or substance combination in the widest sense of the term, preferably pharmaceutical active substances, but particularly preferably agrochemicals which can be used in agriculture or horticulture.

Agrochemicals include fertilizers, herbicides, fungicides, insecticides and other crop protection agents and pesticides, preventive agents, plant growth promoters and inhibitors, silage agents, preservatives, and also soil improvement agents. Feed additives, animal hygiene agents and animal medicaments, and fragrances and flavorings are also included.

For example, use may be made of known active substances as described, for example, in Weed Research 26, 441-445 (1986) or "The Pesticide Manual", 11th edition, The British Crop Protection Council and the Royal Soc. of Chemistry, 1997 and the literature cited therein. Examples of known herbicides which may be introduced in the active substance carriers according to the invention are the following (note: the compounds are either given their common name according to the International Organization for Standardization (ISO) or their chemical name, where appropriate together with a conventional code number): acetochlor; acifluorfen; aclonifen; AKH 7088, i.e. [[[1-[5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrophenyl]-2-methoxyethylidene]amino]oxy]acetic acid and its methyl ester; alachlor; alloxydim; ametryn; amidosulfuron; amitrol; AMS, i.e. ammonium sulfamate; anilofos; asulam; atrazin; azimsulfurone (DPX-A8947); aziprotryn; barban; BAS 516 H, i.e. 5-fluoro-2-phenyl-4H-3,1-benzoxazin-4-one; benazolin; benfluralin; benfuresate; bensulfuron-methyl; bensulide; bentazone; benzofenap; benzofluor; benzoylprop-ethyl; benzthiazuron; bialaphos; bifenox; bromacil; bromobutide; bromofenoxim;

bromoxynil; bromuron; buminafos; busoxinone; butachlor; butamifos; butenachlor; buthidazole; butralin; butylate; cafenstrole (CH-900); carbetamide; cafentrazone (ICI-A0051); CDAA, i.e. 2-chloro-N,N-di-2-propenylacetamide; CDEC, i.e. 2-chloroallyl diethyldithiocarbamic acid; chlomethoxyfen; chloramben; chlorazifop-butyl, chlormesulon (ICI-A0051); chlorbromuron; chlorbufam; chlorfenac; chlorflurecol-methyl; chloridazon; chlorimuron ethyl; chlornitrofen; chlorotoluron; chloroxuron; chloropropham; chlorsulfuron; chlorthal-dimethyl; chlorthiamid; cinmethylin; cinosulfuron; clethodim; clodinafop and its ester derivates (e.g. clodinafop-propargyl); clomazone; clomeprop; cloproxydim; clopyralid; cumyluron (JC 940); cyanazine; cycloate; cyclosulfamuron (AC 104); cycloxydim; cycluron; cyhalofop and its ester derivatives (e.g. butyl ester, DEH-112); cyperquat; cyprazine; cyprazole;

daimuron; 2,4-DB; dalapon; desmedipham; desmetryn; di-allate; dicamba; dichlobenil; dichlorprop; diclofop and its esters, such as diclofop-methyl; diethatyl; difenoxuron; difenzoquat; diflufenican; dimefuron; dimethachlor; dimethametryn; dimethenamid (SAN-582H); dimethazone, clomazon; dimethipin; dimetrasulfuron, dinitramine; dinoseb; dinoterb; diphenamid; dipropetryn; diquat; dithiopyr; diuron; DNOC; eglinazine-ethyl; EL 77, i.e. 5-cyano-1-(1,1-dimethylethyl)-N-methyl-1H-pyrazole-4-carboxamide;

endothal; EPTC; esprocarb; ethalfluralin; ethametsulfuron-methyl; ethidimuron; ethiozin; ethofumesate; F5231, i.e. N-[2-chloro-4-fluoro-5-[4-(3-fluoropropyl)-4,5-dihydro-5-oxo-1H-tetrazol-1-yl]phenyl]ethanesulfonamide; ethoxyfen and its esters (e.g. ethyl ester, HN-252); etobenzanid (HW 52); fenoprop; fenoxan, fenoxaprop and fenoxaprop-P and esters of these, e.g. fenoxaprop-P-ethyl and fenoxaprop-ethyl; fenoxydim; fenuron; flamprop-methyl; flazasulfuron; fluazifop and fluazifop-P and esters of these, e.g. fluazifop-butyl and fluazifop-P-butyl; fluchloralin; flumetsulam; flumeturon; flumiclorac and its esters (e.g. pentyl ester, S-23031); flumioxazin (S-482); flumipropyn; flupoxam (KNW-739); fluorodifen; fluoroglycofen-ethyl; flupropacil (UBIC-4243); fluridone; flurochloridone; fluroxypyr; flurtamone; fomesafen; fosamine; furyloxyfen; glufosinate; glyphosate; halosafen; halosulfuron and its esters (e.g. methyl ester, NC-319); haloxyfop and its esters; haloxyfop-P (= R-haloxyfop) and its

esters; hexazinone; imazamethabenz-methyl; imazapyr; imazaquin and salts, such as the ammonium salt; imazethamethapyr; imazethapyr; imazosulfuron; ioxynil; isocarbamid; isopropalin; isoproturon; isouron; isoxaben; isoxapyrifop; karbutilate; lactofen; lenacil; linuron; MCPA; MCPB; mecoprop; mefenacet; mefluidid; metamitron; metazachlor; methabenzthiazuron; metham; methazole; methoxyphenone; methyldymron; metabenzuron, methobenzuron; metobromuron; metolachlor; metosulam (XRD 511); metoxuron; metribuzin; metsulfuron-methyl; MH; molinate; monalide; monocarbamide dihydrogensulfate; monolinuron; monuron; MT 128, i.e. 6-chloro-N-(3-chloro-2-propenyl)-5-methyl-N-phenyl-3-pyridazinamine; MT-5950, i.e. N-[3-chloro-4-(1-methylethyl)phenyl]-2-methylpentanamide; naproanilide; napropamide; naptalam; NC 310, i.e. 4-(2,4-dichlorobenzoyl)-1-methyl-5-benzyloxypyrazole; neburon; nicosulfuron; nipyraclophen; nitralin; nitrofen; nitrofluorfen; norflurazon; orbencarb; oryzalin; oxadiargyl (RP-020630); oxadiazon; oxyfluorfen; paraquat; pebulate; pendimethalin; perfluidone; phenisopham; phenmedipham; picloram; piperophos; piributicarb; pirifenop-butyl; pretilachlor; primisulfuron-methyl; procyazine; prodiamine; profluralin; proglinazine-ethyl; prometon; prometryn; propachlor; propanil; propaquizafop and its ester; propazine; propham; propisochlor; propyzamide; prosulfalin; prosulfocarb; prosulfuron (CGA-152005); prynachlor; pyrazolinate; pyrazon; pyrazosulfuron-ethyl; pyrazoxyfen; pyridate; pyrithiobac (KIH-2031); pyroxofop and its esters (e.g. propargyl esters); quinclorac; quinmerac; quinofop and its ester derivatives, quizalofop and quizalofop-P and ester derivatives of these, e.g. quizalofop-ethyl; quizalofop-P-tefuryl and ethyl; renriduron; rimsulfuron (DPX-E 9636); S 275, i.e. 2-[4-chloro-2-fluoro-5-(2-propynyloxy)phenyl]-4,5,6,7-tetrahydro-2H-indazole; secbumeton; sethoxydim; siduron; simazine; simetryn; SN 106279, i.e. 2-[[7-[2-chloro-4-(trifluoromethyl)-phenoxy]-2-naphthalenyl]oxy]propanoic acid and methyl ester; sulfentrazon (FMC-97285, F-6285); sulfazuron; sulfometuron-methyl; sulfosate (ICI-A0224); TCA; tebutam (GCP-5544); tebuthiuron; terbacil; terbucarb; terbuchlor; terbumeton; terbuthylazine; terbutryn; TFH 450, i.e. N,N-diethyl-3-[(2-ethyl-6-methylphenyl)-

sulfonyl]-1H-1,2,4-triazole-1-carboxamide; thenylchlor (NSK-850); thiazafluron; thiazopyr (Mon-13200); thidiazimin (SN-24085); thifensulfuron-methyl; thiobencarb; tiocarbazil; tralkoxydim; tri-allate; triasulfuron; triazofenamide; tribenuron-methyl; triclopyr; tridiphane; trietazine; trifluralin; triflusulfuron and esters (e.g. methyl ester, DPX-66037); trimeturon; tsitodef; vernolate; WL 110547, i.e. 5-phenoxy-1-[3-(trifluoromethyl)phenyl]-1H-tetrazole; UBH-509; D-489; LS 82-556; KPP-300; NC-324; NC-330; KH-218; DPX-N8189; SC-0774; DOWCO-535; DK-8910; V-53482; PP-600; MBH-001; KIH-9201; ET-751; KIH-6127 and KIH-2023.

The invention also provides an agrochemical formulation of the novel microparticles. For this, one or more agrochemicals, if desired with formulating auxiliaries or other auxiliaries preferably diatomaceous earth, is introduced into the novel microparticles and formulated and serves preferably for agricultural application.

The invention also provides a pharmaceutical formulation of the novel microparticles. For this, one or more pharmaceutical active substances, if desired together with formulating auxiliaries or other auxiliaries preferably diatomaceous earth, are introduced into the novel microparticles and formulated.

For the purposes of the present invention, "controlled active-substance release" is release of the active substances in a dose advantageous for the biological organism after a particular time and/or period, allowing for some random variation depending on the circumstances.
This definition also includes the extremes of, firstly, spontaneous release of the active substances present in the formulation within a period whose value approximates to zero, and secondly, release of the minimum amount/dose required to

achieve an effect over a long period until all of the active substances present in the formulation have been released.

The synonymous terms depot formulation and formulation with controlled release are therefore used for the present formulation.

The present invention also shows that the release profile can also be modified by selecting suitable matrix materials (Examples 6, 7 and 8 with Figure 1) and/or adding polar formulation auxiliaries or other polar auxiliaries. Adding common salt or cellulose can increase the initial release of active substance (Examples 9 and 10 with Figure 2). Surprisingly, adding diatomaceous earth gives a completely different release profile: significantly more active substance is released over a relatively long period. A further increase in active-substance release is achieved by using specific COC grades (Examples 11, 12 and 13 with Figure 3).

In a preferred embodiment, therefore, matrix materials used for the novel microparticles preferably comprise at least one cycloolefin copolymer selected from polymers containing from 0.1 to 99.9% by weight (based on the total weight of the cycloolefin copolymer) of polymerized units of at least one cyclic olefin and from 0.1 to 99.9% by weight (based on the total weight of the cycloolefin copolymer) of polymerized units of an acyclic olefin.

The matrix materials of the novel microparticles particularly preferably comprise olefins with fundamental norbornene structure, very particularly preferably norbornene or tetracyclododecene. Preference is also given to cycloolefin copolymers which contain polymerized units derived from acyclic olefins with terminal double bonds, for example alpha olefins having from 2 to 20 carbon atoms, and particular preference is given to ethylene or propylene. Norbornene-ethylene and tetracyclododecene-ethylene copolymers are very particularly preferred.

To implement the invention, the matrix materials of the novel microparticles are prepared using heterogeneous or homogeneous catalysis with organometallic compounds. Use may be made of catalyst systems based on mixed catalysts comprising titanium salts and organylaluminum compounds, as described in DD-A-109 224 and DD-A-237 070. EP-A-156464, EP 0 582 355 and EP 0 466 279 describe the preparation with vanadium-based catalysts. EP-A-283 164, EP-A-407 870, EP-A-485 893 and EP-A-503 422 describe their preparation using catalysts based on soluble metallocene complexes. The preparation processes and the catalyst systems described in these patents for preparing cycloolefin copolymers are expressly incorporated herein by way of reference.

They may also be prepared by means of ring-opening polymerization of cycloolefins followed by hydrogenation of the resultant products according to Japanese Patents JP 3-14882, JP 3-122137, JP 4-63807, JP 2-227424 and JP 2-276842. Derivatives of these cycloolefins with polar groups, such as halo groups, hydroxyl groups, ester groups, alkoxy groups, carboxy groups, cyano groups, amido groups, imido groups or silyl groups, are also included.

Mixtures of cycloolefin copolymers and polyolefins are also suitable as matrix materials for the novel microparticles. The following polyolefins may preferably be used here: homopolymers of ethylene and of propylene and copolymers of these; copolymers based on ethylene with linear or branched olefins, such as butene, pentene, hexene, heptene, octene, nonene, decene, undecene or dodecene, and copolymers based on propylene with linear or branched olefins, such as butene, pentene, hexene, heptene, octene, nonene, decene, undecene or dodecene, and terpolymers of ethylene, propylene and linear or branched olefins, such as butene, pentene, hexene, heptene, octene, nonene, decene, undecene or dodecene.

COCs based on comonomers, such as ethylene and 2-norbornene, are amorphous or semicrystalline, transparent materials. The heat resistance of cycloolefin copolymers can be adjusted within a wide range by varying the proportions of the comonomers. The glass transition temperature of cycloolefin copolymers can be used as a guide to their heat resistance, which can be determined on injection moldings in accordance with ISO 75 Part 1 and Part 2 (corresponds to DIN 53461, Deutsches Institut für Normung, Berlin, 9th edition, 1988, p. 198). The cycloolefin copolymers described have glass transition temperatures of from -20 to 220°C.

The average molar mass of the COCs can be controlled by hydrogen feed, varying the catalyst concentration, or varying the temperature, in a known manner. The COCs have weight average molecular masses Mw of from 1000 to 10,000,000 g/mol, preferably from 1000 to 5,000,000 g/mol, particularly preferably from 1000 to 1,200,000 g/mol. The cycloolefin copolymers present in the matrix materials according to the invention for microparticles have viscosity numbers (VN) of from 5 to 1000 ml/g, preferably from 5 to 500 ml/g, particularly preferably from 5 to 300 ml/g.

The matrix materials of the novel microparticles are thermoplastic materials. They may therefore be processed by any of the known processes for processing thermoplastic polymers. These include, inter alia, extrusion of films and fibers, extrusion blow molding of films and bottles, injection blow molding, injection molding and calendering, The flowabilities of the melts can be adjusted, and matched to the conditions for the processing method, by varying the glass transition temperatures and the molar masses.

COCs can also be processed from solution. Suitable solvents are aprotic nonpolar hydrocarbons, such as decalin, or mixtures of linear and branched hydrocarbons.

At temperatures of 300°C, both in extrusion and in injection molding, no decomposition reactions or viscosity degradation were observed.

The properties of the matrix materials of the novel microparticles may be modified either intrinsically or by adding auxiliaries and additives, e.g. plasticizers. Optimized mixtures may comprise, for example, waxes, oils, surfactants, emulsifiers, fats, fibers, fillers or reinforcing agents, active carbon, porous substances, salts, generally polar substances, silicates, zeolites, plasticizers, antioxidants, UV absorbers or light stabilizers, acrylates, nickel compounds, sterically hindered amines, oxalamides, phosphites or phosphonites, peroxide degraders, basic costabilizers, nucleating agents, lubricants, pigments, other colorants, flame retardants, antistats, biostabilizers, optical brighteners, blowing agents, organic peroxides, or also other typical plastics additives and processing aids.

To continue implementation of the invention, various ethylene-norbornene copolymers are mixed by kneading together with the active substance and with fillers, such as common salt, cellulose or diatomaceous earth. The temperature is 100°C. The material is then ground. The particle size is from 100 µm to 1000 µm. The proportion of formulation auxiliaries, other auxiliaries and additives may be from 5 to 50%. The release rates can generally be increased by this means. The concentration of the active substance may be from 1 to 50%. The crop protection agent used is ethoxysulfuron (3-(4,6-dimethoxypyrimidin-2-yl)-1-(2-ethoxyphenoxy-sulfonyl)urea), but the invention is not restricted thereto. The release of the active substance can

be measured in vitro. The release times are from 10 days to about 4 weeks.

Figure 1 shows the active-substance release of the novel microparticles in Examples 6, 7 and 8.

Figure 2 shows the active-substance release of the novel micropraticles in Examples 9 and 10.

Figure 3 shows the active-substance release of the novel microparticles in Examples 11, 12 and 13.

Figure 4 shows scanning electron micrographs of the microparticles at magnification of (a) 200 and (b) 5000.

The following examples serve to describe the invention in greater detail, but without restricting the same to the products and embodiments described in the examples.

Examples

COCs serving as matrix material in the novel microparticles.

Example 1

A 48% strength by weight solution of norbornene in toluene is charged to a 70 dm^3 autoclave previously flushed with ethene. Ethene is repeatedly applied under pressure to saturate the solution with ethene. A toluene-containing solution comprising methylaluminoxane solution (10% strength by weight methylaluminoxane solution with molar mass of 1300 g/mol, determined cryoscopically) is fed in countercurrent to the reactor prepared in this way, and the mixture is stirred at 70°C for 30 minutes. After 30 minutes' preactivation, a solution comprising a total of 30 mg of the metallocene isopropylenebis(1-indenyl)zirconium dichloride in a solution containing toluene was added.

The mixture was polymerized for an hour with stirring while further ethylene was metered in to maintain an ethylene pressure of 20 bar. The amount of hydrogen was 2000 ppm.

At the end of the reaction time the polymerization mixture was discharged into a vessel and immediately introduced into 300 dm^3 of acteone and stirred for 30 minutes, and the precipitated product was then filtered. The filtercake was washed three times alternately with 10% strength hydrochloric acid and acetone; the residue was slurried in acetone and refiltered. The purified product was dried for 24 hours in vacuo (0.2 bar) at 40°C.

This gave a colorless polymer with a VN of 92 ml/g, a glass transition temperature of 80°C and a weight-average molar mass Mw of 52,300 g/mol

This product is termed COC 1 below.

Example 2

The other products were prepared by varying the type of metallocene used, the hydrogen pressure and the amount of norbornene.
A product with a VN of 15 ml/g, a glass transition temperature of 55°C and a weight-average molar mass of 6400 g/mol is termed COC 2.

Example 3

COC 3 is a semicrystalline cycloolefin copolymer with a VN of 70 ml/g, a glass transition temperature of -6°C, a melting point of 69°C and a weight-average molar mass of 34,000 g/mol.

Example 4

37.5 g of COC 1 and 12.5 g of the white oil Ondina G 41 (Shell) were weighed into the mixing compartment, heated to 100°C, of a Haake Rheomix 600 / Rheocord 90 test kneader. The sample was then kneaded (for about 30 minutes) until the torque plotted against time remained constant. The resultant homogeneous product had a glass transition temperature of 15°C. This mixture is termed COC 4 below.

The production of microparticles from COCs of Examples 1 to 4 is described below.

Example 5

To produce the microparticles from cycloolefin copolymers as matrix material a Haake Rheomix 600 / Rheocord 90 test kneader is used. The starting materials are charged under nitrogen to the mixing compartment, heated to 100°C,

of the kneader. The sample is then kneaded at this temperature for 15 minutes at 20 rpm to give a homogeneous mixture. Homogeneous distribution of the components can be discerned in that the torque plotted against time remains constant.

The product is then removed from the kneader, ground in an analytical mill, and separated into various size fractions using screen analysis.

To produce larger amounts, the starting components are charged to the feed pipe of an extruder (Leistritz GL34 twin-screw extruder). The extruder is operated at 100°C and 100 rpm. The yield is about 4 kg/h. An advantage is that the extrudate solidifies very rapidly and can therefore be comminuted quickly. The product is then ground and separated into the desired fractions using screens.

Examples 6 - 13 for the type and amount of the starting components used

6. COC 2: 3.43 g of active substance ethoxysulfuron

7. COC 3: 3.43 g of active substance ethoxysulfuron

8. COC 4: 3.43 g of active substance ethoxysulfuron

9. COC 2: 21.6 g of NaCl and 3.23 g of active substance ethoxysulfuron

10. COC 3: 22.3 g of FIC 200 cellulose fibers and 3.43 g of active substance ethoxysulfuron

11. COC 2: 22.3 g of diatomaceous earth and 3.43 g of active substance ethoxysulfuron

12. COC 3: 22.3g of diatomaceous earth and 3.43 g of active substance ethoxysulfuron

13. COC 4: 22.3 g of diatomaceous earth and 3.43 g of active substance ethoxysulfuron

The release of the active substance is measured via UV absorption. See Examples in Figures 1 to 3.